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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/030,452		Masayuki Yabuta	58777.000008	5707

21967 7590 12/26/2006

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EXAMINER	
ROOKE, AGNES BEATA	
ART UNIT	PAPER NUMBER
1656	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/26/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/030,452	YABUTA ET AL.	
	Examiner	Art Unit	
	Agnes B. Rooke	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-6 and 8-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-6 and 8-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 09/13/2006 has been entered.

The amendments to the claims filed on 09/13/2006 have been acknowledged.

Claims 3-6 and 8-20 are pending. Claims 13-20 are newly added.

Priority

The Applicants claim priority to JAPAN 2000-137228, filed on 05/10/2000, is acknowledged.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claim 11 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 11, the term "byproduct" polypeptide is indefinite since examiner cannot estimate metes and bounds of the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 3-6 and 8-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Hobden et al., UK Patent Application GB 2180539,(published on April 1, 1987).

Hobden et al. teach a hybrid protein comprising a first polypeptide having human ANF. See Abstract; where the DNA mixture derived was used to transform E.coli JM103. See page 10, line 26; where the overnight culture of E.coli JM103 was diluted a hundred-fold into fresh L-broth (30 ml comprises tryptone, yeast extract and NaCl; See page 10, lines 27-28; where the yeast extract is composed of different amino acids (See "Manual of BBL Products and Laboratory Procedures, pages 293-294, see as attached to this office action).

Claims 3-6 and 8-20 are rejected under 35 U.S.C. 102(e) as being anticipated by Ueda et al. (U.S. 2003/0170811 A1).

Ueda et al. teach a process for the production of alpha-human atrial natriuretic polypeptide by recombinant technology. See Abstract.

On page 9, paragraph [0112] teaches expression of a gene coding for the peptide Cla-Fused alpha-hANP (ClaH Protein); where an overnight culture of E.coli H1 containing the expression vector, plasmid pCLaHtrpSd in L-broth, where the E.coli was cultured [0113]; where the L-broth according to the "Handbook of Microbiological Media," (see page 725, as attached to this office action) contains yeast extract, which is composed of different amino acids.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 3-6 and 9-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yabuta et al. (U.S. 5,670,340).

The present invention is directed to a method of producing atrial natriuretic proteins in culture medium or broth that is supplemented with any one of the amino acids histidine, methionine and glycine.

Yabuta et al. teach a process of expression a target peptide in a large amount and accumulation of the target peptide in host cells in the form of occlusion bodies. See Abstract. In Examples 3 and 4, Yabuta et al. teach production of human calcitonin from fusion protein in E.coli. Examples 5-8 teach production of CNP-22 from fusion protein in

E.coli. In column 13, line10, Yabuta et al., teach addition of 2.0 g/L of L-methionine to the culture medium. In column 4, lines 30-32, the preferable host is Escherichia coli.

Yabuta et al. do not teach production of ANP from fusion protein in E.coli.

In column 4, line 20-26, Yabuta et al. state that the method can be applied for production of a fusion protein of physiologically active peptides, for example natriuretic peptides, such as ANP. In Claim 1, Yabuta et al. claim process for the production of a target peptide, where the target peptide can be ANP.

It would have been obvious to a person of ordinary skill in the art to substitute ANP for human calcitonin or CNP as per teachings of Yabuta et al. because the same result should be expected when using ANP in place of CNP or clacitonin. It would be predictable that the method would work with ANP because Yabuta et al. showed that the method was successful with calcitonin and CNP, because Yabuta et al. stated that the same method would work for ANP.

Further, claims 13 and 14 are included in this rejection because in the absence of the evidence to the contrary, the addition of 3.0 g/L of L-methionine as claimed, instead of 2.0 g/L of L-methionine as taught by Yabuta et al. would not make a significant difference in the outcome of reducing formation of a byproduct polypeptide comprising O-acetylserine residue in place of serine.

Claims 11 and 19 are included in this rejection since they refer to a culture medium and such a culture medium is utilized in the method as taught by Yabuta et al, where in the specification Applicants state that any of the amino acids can be used.

Claim 9 is rejected because the preamble states "*a method for reducing formation of a byproduct polypeptide comprising an O-acetylserine residue in place of a serine residue, comprising..*" however the invention only requires culturing transformed host cells in a medium comprising at least one histidine, methionine or glycine in an effective amount to reduce the formation of a byproduct polypeptide. The recitation of o-acetylserine is limited to the preamble of the claims or as the inherent end-point of the claimed method. *In re Hirao*, 535, F.2d 67, 190 USPQ 15 (CCPA 1976), the court states that a preamble does not provide any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness, but instead, the process steps or structural limitation are able to stand alone.

One would be motivated to use ANP in place of calcitonin or CNP because the steps in the method disclosed by Yabuta et al. would be the same, and the expectation of success would be high because of the great results achieved by Yabuta et al. Further, an addition of 3 g/L of L-methionione, instead of 2.0 g/L of L-methionine as taught by Yabuta et al. would be strongly desirable, since the effects of using 2.0 g/L were successful.

In Claims 10-20, the Applicant claims O-acetylserine as a byproduct formed in the method of production of an atrial natriuretic peptide comprising a serine residue.

MPEP section 2106 states that language that suggests or makes optional, but does not require steps to be performed or does not limit a claim to a particular structure, does not limit the scope of a claim or claim limitation. For example, a language that may raise a question as to the limiting effect of the language in a claim are statements of intended use or field of use.

In claims 10-20, the byproduct O-acetylserine has no effect on the steps performed in the method, therefore O-acetylserine does not limit the claims as currently presented.

Therefore, it would have been obvious to one skilled in the art to design a method for the production of a protein comprising culturing E.coli host cells transformed with a plasmid capable of expressing the protein, where the protein produced is the human atrial natriuretic peptide as suggested by Yabuta et al., and where the byproduct formed is in a form of O-acetyl-serine. One would be motivated to produce the atrial natriuretic peptides because of the success of the method in producing a human calcitonin as taught by Yabuta et al.

Applicants arguments and examiner's response

Applicants responded that:

1) the '340 patent is directed primarily to calcitonin or CNP and that there is no discussion of production ANP or any byproducts. In response, examiner points out that

ANP or CNP are both natriuretic peptides and that ANP can be used in the method instead of CNP as taught in the '340 patent.

2) that '340 patent fails to disclose or suggest the specific byproduct polypeptide comprising an O-acetylserine residue in place of a serine residue that occurs when producing ANP; and that it does not teach adding at least one of histidine, methionine, or glycine to reduce the formation of a byproduct polypeptide. In response, examiner points out that the production of O-acetyl-serine as a byproduct would be expected, as part of a cysteine metabolic pathway in E.coli, during the production of a protein comprising culturing E.coli host cells transformed with a plasmid capable of expressing the protein, where the protein produced is a human ANP, as suggested by Yabuta et al. Further, as pointed out on page 17 of the specification, lines 21-26, any one of amino acids: alanine, glycine, serine, methionine or histidine can be added to the suspension of the cell culture in the instant invention, and the Yabuta et al. teach addition of L-methionine, for example.

3) that the Example 3 of the '340 patent does not teach the addition of 2.9 g/L of L-methionine to reduce formation of the byproduct. In response, examiner agrees with Applicants that the reference does not teach addition of 2.9 g/L of L-methionine, since the Example 3 of Yabuta et al. teaches addition of 2.0 g/L of L-methionine. However, in the absence of the evidence to the contrary it would be still obvious to add 3 g/L of methionine instead of 2.0 g/L of methionine to achieve the same goal.

4) that MPEP section 2105 is not relevant to claims 10-12 of the instant invention. In response, examiner agrees with Applicants and states that the relevant

section is MPEP 2106 [R-5] that reads: "The subject matter of a properly construed claim is defined by the terms that limit its scope. It is this subject matter that must be examined. As a general matter, the grammar and intended meaning of terms used in a claim will dictate whether the language limits the claim scope. Language that suggests or makes optional but does not require steps to be performed or does not limit a claim to a particular structure does not limit the scope of a claim or claim limitation" and not the MPEP 2105, as previously cited.

5) that claim 9 recites three method steps, each of which contain the recitation of O-acetylserine byproduct, and thus that examiner improperly limits claim 9. In response, examiner responds that recitation of O-acetylserine is limited to the preamble of the claims or is the inherent end-point of the claimed method. Therefore, the rejection stands.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Agnes Rooke whose telephone number is 571-272-2055. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status

information about the PAIR system, see http://pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197.

AR

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER